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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/126,816	07/31/1998	CHRISTOPH VON EICHEL-STREIBER	PM254992	9336

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	27

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/126,816	VON EICHEL-STREIBER ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 21-29* is/are pending in the application.

4a) Of the above claim(s) *1-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

The Amendment filed January 28, 2003 (Paper No. 26) in response to the Office Action of August 13, 2002 is acknowledged and has been entered.

Claims 1-6, and 21-29 are pending.

Claims 1-6 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 21-29 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All previous rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

New Rejections/Objections:

Claims 21-22, and 25-29 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

Claim 21 is drawn to an isolated polypeptide fragment consisting essentially of approximately the first 1020 N-terminal amino acids of SEQ ID NO:6 for which there is no support in the specification or claims as originally filed. For example, Claim 21 was derived from newly presented Claim 12 in Paper No. 11, page 4 wherein applicants argued that "new

claim 12 is directed to the new and inventive peptide fragment consisting of the first 1020 amino acids of Clostridium sordellii lethal toxin" wherein "the claimed peptide is novel over the prior art". Although the specification teaches (page 10, 2nd paragraph) that a further object of the invention is a "vector" which contains a *nucleotide* acid fragment which codes for the first 1020 amino acids of toxin LT or parts thereof, the claims read on a polypeptide fragment for which there is no clear support in the specification. A vector and nucleic acid product are clearly distinct from a polypeptide fragment since they comprise different chemical entities.

Likewise, claims 22 and dependents thereof are drawn to a compound comprising a polypeptide fragment (the first 1020 amino acids of SEQ ID NO:6) **and** a target cell specific binding domain which permits the compound to bind to a target cell. Thus Claim 22 comprises two parts. However, the specification does not contemplate nor suggest such a compound. The specification only appears to contemplate an "immunotoxin" comprising three parts: a target cell specific binding domain, a translocation domain, and a catalytic domain of the LT toxin (specification, page 4). The specification further teaches (page 7) that an immunotoxin according to the invention is a multidomain protein containing a first part, a second part, and a third part usually connected by covalent bonds.

Claims 22-24, 26, and 28-29 are rejected under 35 USC 102(b) as being anticipated by Popoff (Infection & Immunity, 1987, Vol. 55, No.1, pages 35-43).

For the purposes of comparing the claims to the prior art, the word "compound" is interpreted as meaning a polypeptide.

Popoff teaches as set forth in Paper No. 13, pages 7-8 and Paper No. 10, page 11

Applicants have argued (Paper No. 21, page 11) that the DNA sequence of *Clostridium sordellii* lethal toxin was not known at the time Popoff was published. This argument has been considered but is not found persuasive because applicants admit on the record that Popoff teaches "entire *Clostridium sordellii* lethal toxin proteins" and that "Popoff discloses a method of purifying active lethal toxin (LT) from *Clostridium sordellii*" (Paper No. 21, page 10). Thus, even though Popoff has not described the specific domains of the toxin LT, the claimed compound appears to comprise the same characteristics as to that which is claimed.

Applicants also argue (Paper No. 21, page 10) that Popoff fails to teach a method of obtaining an active fragment of *Clostridium sordellii* lethal toxin. This argument has been considered but is not found persuasive because the claims are not drawn to a specific active fragment, rather the claims encompass a compound (interpreted as a polypeptide) "comprising" a polypeptide fragment of *Clostridium sordellii* lethal Toxin consisting essentially of approximately the first 1020 amino acids of the amino acids sequence of *Clostridium sordellii* lethal Toxin according to SEQ ID NO:6 and a target cell specific binding domain which permits the compound to bind to a target cell and a translocation domain for translocating a catalytic domain of *Clostridium sordellii* lethal Toxin (LT) from the exterior of the cell into the interior of the cell wherein the translocation domain consists essentially of approximately the N-terminal amino acids 1021-1700 of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT). **Inherently**, the

polypeptide of Popoff would comprise such a fragment and such domains since the compound that applicants are claiming is the same as Popoff's. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 22-24 are further rejected under 35 USC 102(a) as being anticipated by Green *et al.* (Gene, 1995, Vol. 161, pages 57-61).

For the purposes of comparing the claims to the prior art, the word "compound" is interpreted as meaning a polypeptide.

Green *et al.* teach a compound "comprising" a polypeptide fragment of *Clostridium sordellii* lethal Toxin consisting essentially of approximately the first 1020 amino acids of the amino acids sequence of *Clostridium sordellii* lethal Toxin according to SEQ ID NO:6 and a target cell specific binding domain which permits the compound to bind to a target cell and a translocation domain for translocating a catalytic domain of *Clostridium sordellii* lethal Toxin (LT) from the exterior of the cell into the interior of the cell wherein the translocation domain consists essentially of approximately the N-terminal amino acids 1021-1700 of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT).

The specification teaches (page 7, 2nd paragraph) that the toxin LT is organized as a single-chained toxin consisting of three domains: The N-terminal domain constitutes the catalytic domain, followed by the intermediary translocation domain, and the final C-terminal region contributing to cellular binding. The specification further notes that the DNA and protein sequence of toxin LT are **described by Green *et al*** and that the catalytic domain of the toxin consists of approximately the first 1020 amino acids of sequence which have the glucosyltransferase activity of LT. Thus, through applicants own admission, the prior art of Green *et al.* clearly anticipates the complete amino acid sequence or polypeptide of the toxin LT. And, because the known polypeptide encompasses a compound "comprising" a polypeptide fragment of *Clostridium sordellii* lethal Toxin [consisting essentially of approximately the first 1020 amino acids of the amino acids sequence of *Clostridium sordellii* lethal Toxin according to SEQ ID NO:6 and a target cell specific binding domain which permits the compound to bind to a target cell and a translocation domain for translocating a catalytic domain of *Clostridium sordellii* lethal Toxin (LT) from the exterior of the cell into the interior of the cell wherein the translocation domain consists essentially of approximately the N-terminal amino acids 1021-1700 of the amino acid sequence of *Clostridium sordellii* lethal Toxin (LT)], the prior art anticipates the claimed compound.

Claims 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Popoff (Infection & Immunity, 1987, Vol. 55, No.1, pages 35-43) in combination with the teaching of Blakey *et al.* (Antibody Toxin Conjugates: A Perspective. Waldmann H. (ed): Monoclonal Antibody Thearpy.Prog.Allergy. Basel, Karger, 1988 vol. 45, pages 50-90) for the reasons of record in Paper No. 13, pages 12-13.

Since applicant's arguments addressing the Popoff reference are substantially the same as those presented above, the rejection is maintained. Essentially, although the Popoff reference does not characterize the domains of the lethal toxin, the reference does teach the isolation of LT and a pharmaceutical composition comprising LT. Since the LT polypeptide inherently "comprises" the specifically claimed fragments and domains, the prior art of Popoff is applicable to the instant rejection.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
February 10, 2003